Isohexide and sorbitol-derived, enzymatically synthesized renewable polyesters with enhanced T_g

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ABSTRACT

Sugar-based polyesters derived from sorbitol and isohexides were obtained *via* solvent-free enzymatic catalysis. Pendant hydroxyl groups, coming from the sorbitol units, were present along the polyester backbone, whereas the two isohexides, *viz*. isomannide and isoidide dimethyl ester monomers, were selected to introduce rigidity into the polyester chains. The feasibility of incorporating isomannide as a diol compared to the isoidide dimethyl ester as acyl-donor *via* lipase-catalyzed polycondensation was investigated. The presence of bicyclic units resulted in enhanced T_g with respect to the parent sorbitol-containing polyester lacking isohexides. The different capability of the two isohexides to boost the thermal properties confirmed the more flexible character provided by the isoidide diester derivative. Solvent-borne coatings were prepared by cross-linking the sugar-based polyester polyols with polyisocyanates. The increased rigidity of the obtained sugar-based polyester polyols led to an enhancement in hardness of the resulting coatings.

1. INTRODUCTION

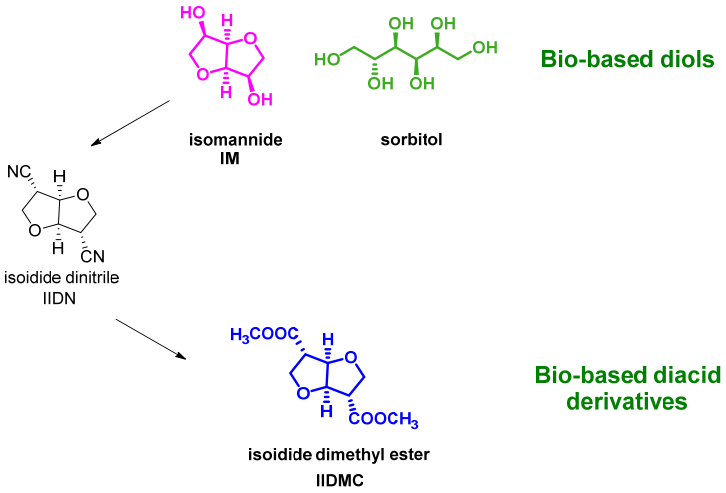
Biomass from renewable resources is the cutting-edge feedstock for the production of novel building blocks for polymers with outstanding performance. Carbohydrates stand out among others since they are one of the most abundant types of biomass from which a wide range of bio-based monomers can be easily obtained. However, one of the major drawbacks of directly using native carbohydrates in the synthesis of polymeric materials is their limited thermal stability, mainly caused by the multifunctional nature of the compounds, the functionalities for instance being multiple hydroxyl groups.[1] Thus, the use of raw carbohydrates for the high temperature bulk synthesis of sustainable polymers is still challenging.

Being part of the "top twelve renewable building blocks", sorbitol has been identified as a potential key chemical intermediate from biomass resources. Already widely used in the food industry, but also as a chemical platform for the production of isosorbide,[2] sorbitol appears to be a good candidate to yield hydroxyl-functionalized aliphatic polyesters.[3,4,5] However, conventional catalysts used in polycondensation reactions usually require relatively high temperatures, at which sorbitol may not be thermally stable.[6] In our previous work it has been demonstrated that, compared with conventional catalysts, the use of *Candida Antarctica* lipase B (CALB) as biocatalyst leads to the most suitable approach for the synthesis of polyesters with preserved sorbitol units.[7] In fact, when sorbitol is copolymerized together with the bio-based 1,3-propanediol (1,3-PD) and potentially bio-based dimethyl adipate (DMA), sorbitol is reacting mainly through its primary hydroxyl groups, thus leaving pendant (secondary) hydroxyl groups in the obtained polyesters available for further modifications, e.g. for the curing reaction with polyisocyanates to obtain poly(ester urethane)s. However, the resulting sorbitol-based aliphatic polyesters showed low glass transition temperatures (T_g), well below room temperature, limiting their range of applications.

Monocyclic and bicyclic monomers derived from sugars, such as acetalized sugar-derivatives[8,9] and dianhydro sugar-derivatives, are known to dramatically enhance the T_g of the obtained polyesters while increasing sustainability.[10,11,12,13] The dianhydro hexitols, also known as isohexides, are a group of highly promising renewable secondary rigid diols, which are directly obtained by the dehydration of sugar alcohols, yielding three isohexide isomers: isosorbide (1,4:3,6-dianhydro-D-glucitol), isoidide (1,4:3,6-dianhydro-D-iditol) and isomannide (1,4:3,6-dianhydro-D-mannitol). Despite the apparent advantages of incorporating rigid monomers such as isohexides into the polymer it is known that, under conventional melt polymerization conditions, the secondary hydroxyl groups of 1,4:3,6-dianhydrohexitols display reduced reactivity hampering so far the large scale industrial applications in the polymer field.[14,15] The synthesis of more reactive isohexide derivatives such as amines[11,16] or

isocyanates[17,18] has been considered as an alternative strategy for the incorporation of the isohexide monomers into polycondensation polymers. Recently, a 1-carbon extended isohexide derivative with methyl ester functionality, namely isoidide dimethyl ester (IIDMC), has been reported as a comonomer for the synthesis of sugar-based polyesters with enhanced T_g.[19] So far, polymerizations involving this novel monomer were only performed using conventional metal-based catalysts.

The aim of this work is to obtain aliphatic polyesters with enhanced T_g and having pendant hydroxyl-functional groups along the polymer chain, *via* an eco-friendly solvent-free enzymatic polycondensation method. The structures of the sugar-derived monomers involved in this study are depicted in Scheme 1. The feasibility of incorporating isohexides either as alcohol donor or acyl donor will be investigated. Additionally, a systematic structure-thermal properties study of the obtained polyesters based on mol% of rigid isohexide building block incorporated will be conducted. The obtained hydroxyl-functional sugar-based polyesters will be cured with conventional petroleum-based and with bio-based hydroxyl-reactive curing agents and tested as solvent-borne coatings.



Scheme 1. Structures of the sugar-derived monomers.

2. EXPERIMENTAL SECTION

2.1. Materials

Sorbitol was obtained as a gift from Roquette (NeosorbP6 Sorbitol, 98%). 1,3-propanediol (1,3-PD, 98%), dimethyl adipate (DMA, >99%), isomannide (IM, 95%), acetic anhydride (>99%), chromium (III) acetylacetonate ($Cr(acac)_3$, 99.99%), 2-chloro-4,4,5,5-tetramethyldioxaphospholane (95%), chlorotrimethylsilane (>99%) and an 0.1–0.5 N methanolic solution of KOH were obtained from Sigma-Aldrich. Isomannide was purified by recrystallization from ethanol with final purity >99.5% (^{13}C

NMR). Solvents were purchased from Biosolve and all chemicals were used as received. Chloroform-*d* (99.8% atom-d) and pyridine-d_5 (99.5% atom-d) were obtained from Cambridge Isotope Laboratories. Ethyl ester L-lysine diisocyanate (EELDI, 95% pure) was supplied by Infine Chemicals Co., Limited, China. The isocyanurate trimer of hexamethylene diisocyanate (Desmodur N3600) was a kind gift from Bayer AG. The polyisocyanates were kept in the fridge at 4 °C under argon. SPRIN liposorb CALB (*Candida antarctica* lipase B, immobilized on beads of a divinylbenzene (DVB)-cross-linked, hydrophobic, macroporous polymer based on methacrylic esters), was purchased from SPRIN S.p.a. and stored in a refrigerator at 4 °C. Like sorbitol and IM, the biocatalyst was dried before use at room temperature under reduced pressure for 24 h following a literature procedure.[3]

2.2. Synthesis of (3S,6S)-dimethyl hexahydrofuro[3,2-b]furan-3,6-dicarboxylate (IIDMC) monomer

According to a reported procedure, isoidide dinitrile (IIDN) was synthetized from isomannide.[19] IIDN was further converted into (3S,6S)-dimethyl hexahydrofuro[3,2-b]furan-3,6-dicarboxylate (IIDMC). In a 100 mL one-necked round-bottom flask equipped with a magnetic stirrer and a reflux condenser, methanol (20-40 mL), HCl (32%, 20-40 mL), and IIDN (1,5-3 g) were sequentially charged. After stirring at reflux for 5 h, the reaction mixture was cooled to room temperature and extracted with chloroform (3 x 50-60 mL). The combined organic layers were dried over $MgSO_4$ and filtered through a glass filter (pore size 4). The resulting solution was evaporated under reduced pressure by rotary evaporation to yield slightly yellowish oil as crude product. Pure IIDMC was obtained as a colorless liquid by flash column chromatography (ethyl acetate: petroleum ether = 1:5). Yield: 72% (purity 95%, ^{13}C NMR). ^{13}C NMR ($CDCl_3$): δ (ppm)= 4.92 (s, 2H), 4.10 (m, 2H), 3.73 (s, 6H), 3.20 (t, 2H).

2.3. Synthesis of sugar-based polyesters

Sugar-based polyesters were obtained from a mixture of sorbitol (5 mol%), 1,3-PD and DMA with the selected composition of 0, 5, 10, 26, 38 and 46/49 mol% of the bicyclic isohexide substituting either 1,3-PD by IM, or DMA by IIDMC. In a 100 mL three neck round bottom flask with a magnetically coupled half-moon stirrer, 1,3-PD, sorbitol, DMA and either IM or IIDMC were melted at 105 °C. When a clear reaction mixture was obtained, the temperature was set to 98-100 °C and the catalyst (7 wt% of SPRIN liposorb CALB with respect to the total amount of monomers) was added to the reaction mixture. The reaction mixture was stirred at 120 rpm for 2-16 h (increasing time with increased amount of IM) under a constant argon flow, aiding the produced condensate methanol to pass over a vigreux column and to condensate in a Dean-Stark apparatus. After the pre-polymerization step, the reaction was continued under reduced pressure descending from 300 mbar to 80-50 mbar over 4-16 h, and subsequently was continued at 80-50 mbar till the end of the polymerization. Regarding the

polymerization of IM with IIDMC only, the removal of the side-products was executed through a gentle flow of argon without applying reduced pressure. After that time, the flask was cooled down to room temperature at atmospheric pressure and the reaction was quenched by adding approx. 10 mL of chloroform. The resulting mixture was filtered through a glass filter (pore size 1) to separate the crude product solution from the enzyme beads. Further workup included the precipitation of this solution in cold methanol. The white-colorless or yellowish material obtained after precipitation was isolated by decantation as a viscous sticky honey-like material residing at the bottom of the flask and dried under reduced pressure overnight at 25 °C.

2.4. Preparation of solvent-borne coatings

The hydroxyl-functional sugar-based polyesters were dried in a vacuum oven at 25 °C at least for 24 hours before being cured using two different poly- and di-isocyanates: i) a trimer of hexamethylene diisocyanate (trifunctional polyisocyanate, NCO equivalent weight = 183 g/mol, known as Desmodur N3600), and ii) the ethyl ester of L-lysine diisocyanate (difunctional polyisocyanate, NCO equivalent weight = 113 g/mol, EELDI). A solution of 0.15 g of the sugar-based polyester in 0.2 mL of chloroform was prepared and added to the pure isocyanate (1:1 equivalent ratio of NCO relative to the amount of OH-groups present in the sample and corrected based on the factor observed between OHV from potentiometric titration and ^{31}P NMR spectroscopy for entry **a**).[7] The obtained two-component mixture was then applied onto a pre-cleaned aluminum Q-panel with a wet film thickness of 160 µm using an adjustable doctor blade. The films were dried at room temperature for 30 min followed by one hour at 80 °C under argon, and cured for 30 min at 150 °C under argon. The films from poly(propylene-*co*-sorbitol adipate) (entry **a**) were obtained by using *N*-methyl-2-pyrrolidone (NMP) as a solvent, dried at 80 °C under argon and cured for 30 min at 180 °C under argon. The coatings were tested for hardness, reverse impact resistance and solvent resistance. The free standing films for DSC measurements were prepared by solubilizing 0.15 g of sorbitol-based polyester in 0.2 mL of chloroform, and subsequently adding it to an exact amount of pure curing agent (1:1 ratio between NCO and OH reactive groups). *Via* a syringe, the solution was applied on a Teflon substrate. The wet films were dried at 80 °C under argon, and cured for 30 min at 150 °C under argon atmosphere.

2.5. Characterization methods

Size exclusion chromatography (SEC). SEC in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) was performed on a system equipped with a Waters 1515 Isocratic HPLC pump, a Waters 2414 refractive index detector (35 °C), a Waters 2707 auto sampler, and a PSS PFG guard column followed by two PFG-linear-XL (7 µm, 8 × 300 mm) columns in series at 40 °C. HFIP with potassium trifluoroacetate (3

g/L) was used as eluent at a flow rate of 0.8 mL/min. Before SEC analysis was performed, the dissolved samples were filtered through a 0.2 μm PTFE filter. The molecular weights were calculated against poly(methyl methacrylate) standards (Polymer Laboratories, Mp = 580 Da up to Mp = 7.1 × 106 Da).

Carbon nuclear magnetic resonance (^{13}C NMR). Quantitative ^{13}C NMR spectroscopy was performed on a Bruker AMX-300 spectrometer at 25.0 °C, operating at 75.5 MHz using an inverse gated decoupling pulse sequence to avoid nuclear Overhauser effect (nOe) enhancement of the ^{13}C NMR signals. Around 15000 scans were acquired with 64K data points and a relaxation delay of 3 s. The spectral width was 22727 Hz and the number of data points for the FID was 32K. Samples were prepared by dissolving 40-50 mg of the crude polymer in 0.5 mL pyridine-d_5 and adding $Cr(acac)_3$ (0.025 M) as a spin relaxation agent. Chemical shifts are reported in ppm relative to the residual peak of pyridine-d_5 (δ = 135.91 ppm). Data analysis was performed using Mestrec 4 software.

Phosphorus nuclear magnetic resonance (^{31}P NMR). ^{31}P NMR spectroscopy was performed on a Varian Unity Inova 500 spectrometer at a resonance frequency of 202.34 MHz. The spectral width of the experiments was 53569.79 Hz. The delay time was set at 3 s with a number of recorded scans of 1024. Sample preparation was carried out following a literature procedure.[20] A stock solution was prepared by weighing exactly 530 mg $Cr(acac)_3$ (30.3 mM) and 150 mg cyclohexanol (30 mM) in a 50 mL volumetric flask. These compounds were subsequently dissolved in a mixture of pyridine and $CDCl_3$ (2.3:1 volume ratio). 4Å molecular sieves were added to protect the stock solution against moisture. Cyclohexanol was used as an internal standard for quantification purposes. Around 45-50 mg of the polymer was accurately weighed into a vial, 0.6 mL of stock solution was added and the solution was transferred to a 5 mm NMR tube. Subsequently, 70 μL of phospholane reagent was added and HCl gas was formed, indicating that the phosphorylation reaction took place. The reaction mixture was left to react for about 30 min at room temperature. Upon completion of the reaction, after the HCl formation had stopped, the solution was used to obtain the ^{31}P NMR spectra. Chemical shifts are reported in ppm relative to the residual peak of water-derivatized phospholane (δ = 132.2 ppm). Data analysis was performed using Mestrec 4 software. Data afforded by the experiments are expressed in mg KOH/g sample in order to simplify the calculation of the curing reagents.

$$Carboxylic\ groups\ \left(\frac{mg\ KOH}{g\ sample}\right) = \frac{mg_{cyclohexanol} \cdot \frac{56100\ mg\ KOH}{mol\ KOH} \cdot peak\ area\ carboxylic\ group}{mg_{polyester} \cdot \frac{100.2\ g\ cyclohexanol}{mol\ cyclohexanol} \cdot peak\ area\ cyclohexanol}$$

$$Hydroxyl\ groups\ \left(\frac{mg\ KOH}{g\ sample}\right) = \frac{mg_{cyclohexanol} \cdot \frac{56100\ mg\ KOH}{mol\ KOH} \cdot peak\ area\ hydroxyl\ group}{mg_{polyester} \cdot \frac{100.2\ g\ cyclohexanol}{mol\ cyclohexanol} \cdot peak\ area\ cyclohexanol}$$

$$OHV = AV + OHV_{sorbitol} + OHV_{Isomannide} + OHV_{1,3-Propanediol}$$

Thermogravimetric analysis (TGA). TGA was performed using a TA Instruments TGA Q500. The analysis of the data was performed with the Universal Analysis 2000 software. A sample of 10 mg was heated from 25 ºC to 600 ºC at a heating rate of 10 ºC/min under nitrogen flow.

Differential scanning calorimetry (DSC). DSC was performed with a TA Instruments Q100 DSC. The heating and cooling rates were 10 °C/min under a nitrogen atmosphere. For the data analysis, Universal Analysis 2000 software was used.

2.6. Evaluation of coating performance

The obtained coatings were evaluated using several characterization methods. The solvent resistance of the coatings was assessed through the acetone rub test, in which the sample is rubbed back and forth with a cloth drenched in acetone. If no damage is visible after more than 150 rubs (*i.e.* 75 'double rubs'), the coating has good acetone resistance. Resistance against rapid deformation was tested using the reverse impact test, performed by dropping a weight of 1 kg on the back of a coated panel from a height of 80 cm (ASTM D2794)[21]. The coating hardness was measured using the pencil hardness test, performed by scratching the coating with pencils of increasing hardness using an Elcometer 501 Pencil Hardness Tester. The coating thicknesses were measured through magnetic induction using an Elcometer 224 Digital Surface Profile Gauge.

3. RESULTS AND DISCUSSION

3.1. Substrate specificity of *Candida Antarctica* lipase B (CALB) for isohexide-derived monomers

As a lipase, in nature CALB is responsible for the hydrolysis of fatty esters. In organic media, lipases can be active in the reverse reaction and accept alcohols as nucleophiles for the formation of ester bonds.[22] In the synthesis of polyesters, CALB shows high activity when linear apolar monomers are involved in the reaction, due to their structural similarity with its natural substrates, *i.e.* triglycerides. The active site crevice of CALB can be partitioned into two sides, an acyl-acceptor pocket and an

alcohol-acceptor pocket, where the corresponding parts of the substrate will be located during catalysis.

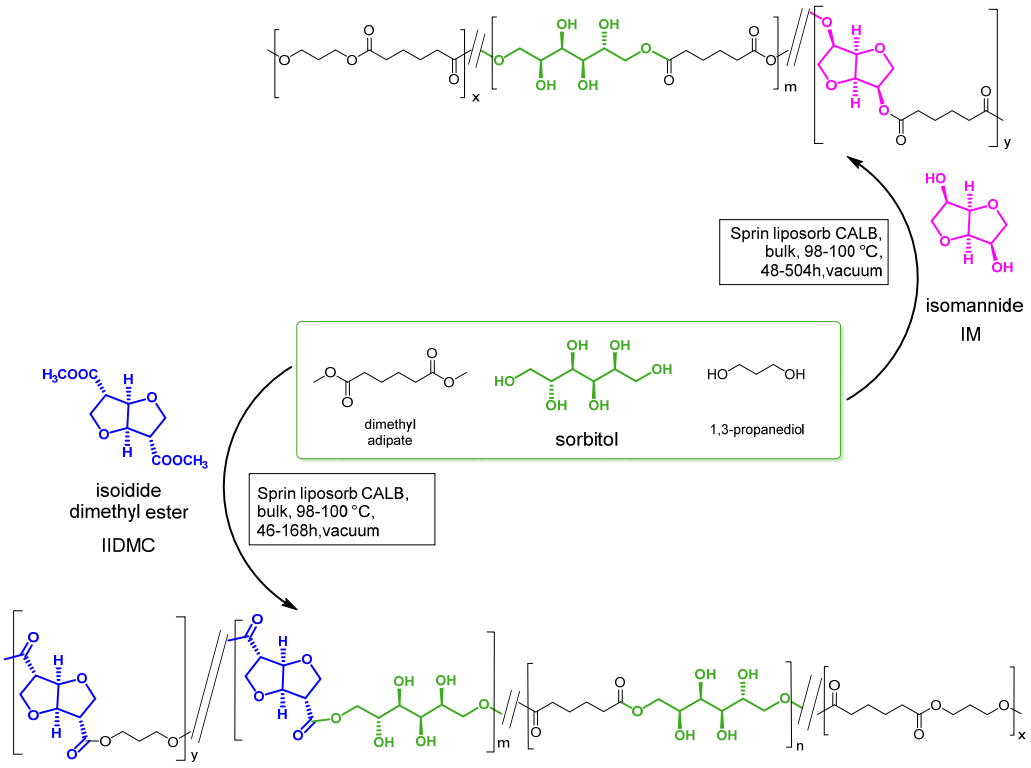
A limited available space in the active site of the alcohol binder pocket makes α,ω-aliphatic linear diols excellent substrates for CALB,[23,24] while secondary alcohols are accepted depending on the size of the substituent, the acceptance being higher for short linear chains[25] than for bulky substituents.[26] Thus, the reaction rate for bicyclic monomers with secondary alcohols is lower compared with linear monomers with primary alcohols, making unmodified isohexides not the favorite diol substrates in a lipase-catalyzed reaction. Besides displaying regio-selectivity for primary over secondary hydroxyl groups, CALB exhibits pronounced enantio-selectivity for the R-configuration toward the S-configuration of secondary hydroxyl groups.[22,27,28] Among the unmodified isohexide isomers, isomannide (IM) is the only one where both secondary hydroxyl groups display R-configuration and the *endo*-hydroxyl groups are in the most appropriate direction to form hydrogen bonding in the transition state of CALB.[29] On the other hand, chemo-selectivity of CALB for the acyl donor substrate is not as strict as for the alcohol group. In fact, in a study comparing substrate specificity between different lipases, CALB was classified as a lipase with a large acyl binder cleft and narrow alcohol binding cleft, this being the reason for its high selectivity for the alcohol substrates with respect to the acyl donor group.[30]

The synthetic path provided by Wu *et al.* for the synthesis of the 1-carbon extended isohexide monomer, *i.e.* isoidide dimethyl ester (IIDMC), starts from IM and modifies the secondary hydroxyl-groups to the highly reactive dinitrile derivative with inverted configuration of the stereocenters.[19] Afterwards, the obtained *exo-exo* isoidide dinitrile (IIDN), *via* methanolysis reaction, is converted into the corresponding dimethyl ester derivative IIDMC. The convenience in using the dimethyl ester form of the isoidide-derived monomer instead of the corresponding dicarboxylic acid is clearly supported by the requirement of only one synthetic step from the isoidide dinitrile intermediate, and the production of methanol during the polycondensation reactions as an easily removable condensate instead of water. Therefore, IM and IIDMC are the isohexide-based compounds chosen in the present study.

3.2. Enzymatic synthesis of the sorbitol- and isohexide-based polyesters

Two series of copolyesters containing sorbitol, and either IM or IIDMC as rigid diol or rigid dicarboxylate units, respectively, have been synthesized *via* enzymatic solvent-free polycondensation (Scheme 2). 1,3-propanediol (1,3-PD) and dimethyl adipate (DMA) have been used as comonomers, since the polarities of these (potentially) bio-based monomers are adequate to provide a homogeneous reaction mixture with IM and/or IIDMC, and thus to favor interactions with CALB in

solvent-free conditions. Commonly, lipase-catalyzed reactions are performed by using 10 wt% with respect to the total amount of monomers of an immobilized form of CALB known as Novozyme 435. To achieve comparable activity, 7 wt% of SPRIN liposorb CALB with respect to the total amount of monomers is used as biocatalyst in this study.[5] With the aim of obtaining polyesters with molecular weights and functionalities suitable for coating applications, implying M_n values between 3 and 6 kg/mol, the Carothers equation was used to estimate the M_n expected for a certain composition, assuming that sorbitol would react as a diol. The polymerizations were performed aiming to obtain hydroxyl end-capped polyesters by using an excess of diols. Thus, all the reaction mixtures contained 51 mol% of diols and 49 mol% of the dimethyl ester comonomers (Table 1).



Scheme 2. Schematic representation of the two series of reactions involving IM as diol and IIDMC as dicarboxylic methyl ester.

In order to obtain polyesters with an adequate amount of pendant hydroxyl groups and a suitable hydroxyl value (OHV) for coating applications, 5 mol% of sorbitol with respect to the total amount of monomers was maintained for all the polymerizations performed in this study, except for the reaction where only bicyclic monomers are used as comonomers (entry **g**, Table 1). A reference poly(propylene-*co*-sorbitol adipate) (entry **a**, Table 1) lacking bicyclic units but also containing 5 mol% of sorbitol was synthesized for comparison purposes. Regarding the first series of polycondensation reactions, 1,3-PD was partially or totally replaced by IM with contents ranging from 5 to 46 mol% (entries **b** to **f**, Table 1). Regarding the second series, DMA was partially or totally replaced by IIDMC with contents ranging from 5 to 49 mol% (entries **B** to **F**, Table 1). To facilitate further comparison

between reactions starting with comparable initial molar feed composition of bicyclic units, entries have been named in lowercase for the IM-containing series and uppercase for the analogous compositions in the IIDMC-containing series. The only difference in the initial feed composition of bicyclic units is related to entries **f** and **F**. In entry **f**, 1,3-PD was fully substituted by IM while sorbitol was maintained at 5 mol% with respect to the total amount of monomers. Therefore the maximum mol% of rigid monomer in the feed in this series was 46 mol% of IM. Conversely, in entry **F** dimethyl adipate was fully substituted by IIDMC, also maintaining 5 mol% sorbitol, but the mol% of rigid monomer was 49% of IIDMC in this case.

Table 1. Molar composition and molecular weights of sugar-based polyesters.

								^{13}C NMR	SEC	
Entry	Initial feed composition (mol%)[a,b]		Reaction time (h)	Yield (%)	Sorbitol incorporated (mol%)[c]	IM incorporated (mol%)[c]	IIDMC incorporated (mol%)[c]	M_n (kg/mol)[d]	M_n (kg/mol)[e]	PDI[e]
	Diesters	Diols								
	DMA	PD:Sorb:IM								
a	49	46: 5: 0	24	64	3.4	0	0	5.4	12.2	2.6
	DMA	PD:Sorb:**IM**								
b	49	41 : 5 : **5**	48	68	3.5	3.7	0	1.2	13.8	3.0
c	49	36 : 5 : **10**	48	62	3.0	3.5	0	1.1	16.6	2.7
d	49	20 : 5 : **26**	55	54	4.3	17.8	0	1.1	6.3	4.4
e	49	8 : 5 : **38**	124	52	3.7	38.6	0	1.3	7.1	2.1
f	49	0 : 5 : **46**	504	20	5.0	42.2	0	1.0	1.4	1.6
	IIDMC:DMA	PD:Sorb								
B	**5** : 44	46 : 5	48	64	3.7	0	5.8	1.1	4.5	3.3
C	**10** : 39	46 : 5	72	55	2.7	0	13.0	1.1	6.2	2.6
D	**26** : 23	46 : 5	46	72	3.7	0	29.0	1.3	8.9	2.5
E	**39** : 10	46 : 5	72	57	3.6	0	45.1	1.8	5.3	2.3
F	**49** : 0	46 : 5	168	70	2.1	0	55.7	1.2	4.2	1.8
	IIDMC	**IM**								
g	**45.5**	**54.5**	139	35	0	49	51	0.7	1.3	1.2

[a]: DMA = dimethyl adipate; PD = 1,3-propanediol; Sorb = sorbitol; IM = isomannide; IIDMC = isoidide dimethyl ester. [b]: Mol% calculated by dividing the amount of monomer by the total amount of comonomers in the feed. [c]: Molar composition in the copolyester as determined by ^{13}C NMR analysis. [d]: Based on the ^{13}C NMR area of end-groups present in the polyesters after precipitation in MeOH. [e]: Based on SEC measurements in HFIP of the precipitated polyesters.

The relatively polar 1,3-PD compound and sorbitol should provide, together with the rather polar IM or IIDMC, a homogeneous phase when mixed with DMA. Although two phases were clearly observed with increasing amounts of IM or IIDMC in the initial feed, within 15 minutes under stirring conditions at 98-100 °C under argon flow a homogeneous mixture was obtained, and then the biocatalyst SPRIN liposorb CALB was added. In the first step, transesterification leading to oligomers was accomplished

under gentle argon flow during 2 to 4 hours. Afterwards, maintaining the same temperature, reduced pressure was applied starting from 300 mbar and slowly decreasing to 80 mbar in 16 hours. The pressure was then settled to 80 mbar and maintained till the end of the polymerization. Those gentle conditions were selected considering an efficient removal of the methanol formed during the pre-polymerization step and to favor the formation of products but taking into account the high volatility of the isohexides and 1,3-PD.[15]

All sugar-based polyesters were obtained as honey-like materials, except for entry **g** which resulted in a fine white powder. The recorded yields were ranging from 20 to 72% after purification by precipitating the crude product in cold methanol. The molecular weights and polydispersities of the final polymers after precipitation in methanol were analyzed by SEC. The resulting sugar-based polyesters displayed M_n values in the range between 1 and 17 kg/mol, with polydispersities (PDIs) between 1.6 and 4.4 (Table 1). In general, the PDI of the two series are comparable. Due to the low reactivity of IM in the lipase-catalyzed polycondensation reaction, longer reaction times were necessary, at which not only IM was easily sublimated but also 1,3-PD was prone to evaporate as well. The presence of white crystals on the top of reactor corresponding to IM-DMA dimers sublimated during the reaction explained the low yield of these polymerizations. When 1,3-PD was totally replaced by IM (entry **f** in Table 1), low molecular weights were obtained even after 504 hours of reaction, with a yield of only 20%, confirming the low reactivity of IM with respect to the other monomers. More satisfactory results were obtained when IIDMC was used as rigid monomer. Shorter reaction times showed to be sufficient to achieve the desired molecular weights. When DMA was totally replaced by IIDMC (entry **F**), longer reaction times were necessary, although much shorter than in the case of the same amount of rigid units totally replacing 1,3-PD (entry **f**), evidencing the higher reactivity of IIDMC as acyl donor with respect to IM as diol. No evidence of sublimation was observed in the reactions involving IIDMC.

Thermogravimetric analyses (TGA) of the pure isohexides, *i.e.* IM and IIDMC, have been carried out to compare their thermal stability. The experiment was conducted equilibrating the sample at 100 °C under nitrogen flow and maintaining at this temperature for 12 hours. In the case of IM, all the monomer was sublimed after one hour at 100 °C, while for IIDMC 8 hours at the same temperature were necessary for complete evaporation. Although the TGA experiments are far from mimicking the polymerization reaction conditions, with this experiment the lower volatility of IIDMC with respect to IM was proved. The high volatility of IM is also a limiting factor to permit full conversion of this diol into a polyester under solvent-free enzymatic polycondensation reaction conditions. It has already been

reported that melt polycondensation provides some limitations regarding the incorporation of unmodified isohexides due to distillation occurring during reaction.[15]

A successful attempt to enzymatically polymerize the two bulky monomers, *viz.* IM and IIDMC, to obtain fully isohexide-based polyesters was achieved. To avoid any loss caused by too severe reaction conditions, no reduced pressure was applied in this case, but only a gentle argon flow was used for the removal of the side product. The high viscosity of the reaction mixture in the solvent-free approach after 138 hours was the limiting factor for obtaining higher M_n. Although this reaction yielded only oligomers, these results are comparable with those reported by Wu *et al.*[31] who used conventional metal-based catalysts at higher temperature. Contrary to isohexide-based polyesters obtained *via* conventional, high temperature metal-based catalysis, *via* enzymatic catalysis the final products resulted in colorless or merely slightly yellow materials. Discoloration of isohexide-based polyesters is a typical effect occurring when reactions are performed at high temperature.[31] It must be highlighted that for the first time IIDMC has been used as acyl-donor in enzymatically catalyzed polyesterifications and, due to the relatively flexible conformation for the acyl-donor moiety of the CALB active site, IIDMC can be considered to be a promising rigid monomer for enzymatic polycondensation reactions.

3.3. Molecular characterization of sugar-based polyesters

Detailed molecular characterization was performed with the aim to evaluate the feasibility and efficiency for the incorporation of the different sugar-based monomers into the polyesters *via* enzymatic polycondensation. The chemical compositions of the polyesters were determined *via* inverse-gated decoupling ^{13}C NMR spectroscopy. The ^{13}C NMR spectra corroborated the chemical structure of the polyesters with all signals being assigned to the carbons contained in the repeat unit. Representative spectra are depicted in Figures 1 and 2, corresponding to polymerization reactions starting from 26 mol% of the bicyclic monomers IM and IIDMC, respectively. Integration of the signals arising from adipate, 1,3-PD, sorbitol, IM and IIDMC units led to the quantification of the compositions of the copolyesters after precipitation in cold methanol. The mol% of the sugar units, *i.e.* sorbitol, IM and IIDMC, present in the precipitated polyesters are gathered in Table 1. The sorbitol content was between 2 and 5 mol%. Regarding copolyesters synthesized using IM as diol, a clear trend can be observed. An increased initial feed of IM led to higher amounts of IM in the final polyester, except for entries **b** and **c**, but differing in all cases from the initial feed composition. The selective CALB biocatalyst favors the incorporation of primary alcohols, *i.e.* 1,3-PD and sorbitol through its primary OH groups, while the less reactive IM is only incorporated at high conversions. When IM is present as minor comonomer, *i.e.* its molar percentage in the feed is equal to or below 10% (entries **b** and **c**),

only a minority of the IM in the feed is incorporated into the polyesters. However, when reducing the amounts of the more reactive 1,3-PD, the less reactive IM is forced to be incorporated into the copolyester, although with mol% being lower than the mol% corresponding to the feed composition and requiring much longer reaction times. Although it is assumed that by dissolution/precipitation from chloroform/methanol the residual monomers are removed due to its solubility in a polar solvent such as methanol, peaks due to unreacted IM monomer have been detected in the ^{13}C NMR spectra, as indicated in Figure 1. When the polymer product is not a solid, effective removal of monomers is challenging and may require successive precipitations which can be a limiting factor in low scale reactions. Nevertheless, since the ^{13}C NMR signals corresponding to pure IM have been assigned, an accurate calculation of the IM residues effectively incorporated into the polymer chains was possible, providing reliable results. The formation of ester bonds involving IM units was also evident from signals related to the neighboring units. The signal of the methylene group next to the carbonyl group of the adipate unit (at 34 ppm, ∇) appears to be split into two peaks, distinguishing the two situations when the adipate unit is either attached to a 1,3-PD unit (34.2 ppm) or to IM (33.9 ppm). A similar behavior can be also observed for the quaternary carbon of the carbonyl group at 173-174 ppm, presenting three distinct signals depending on the diol attached to the adipate unit, *i.e.* sorbitol, 1,3-PD or IM (Figure S1).

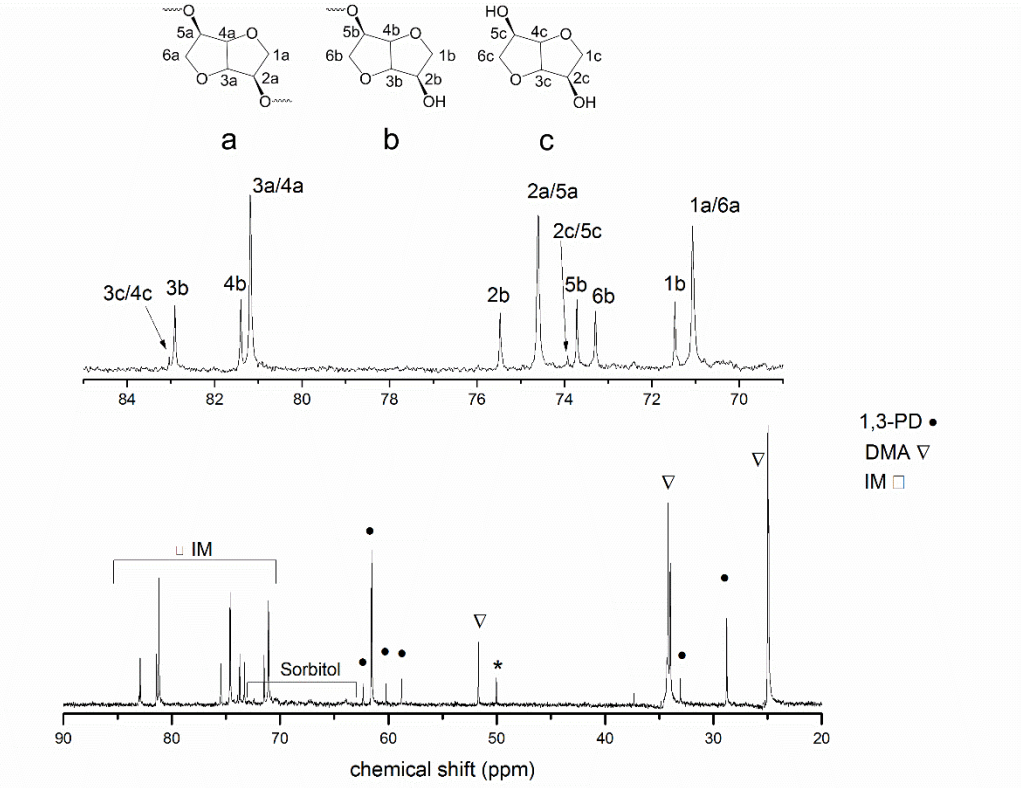


Figure 1. Section of inverse-gated decoupling ^{13}C NMR spectrum of entry **d** in Table 1 recorded in pyridine-d_5. Assignment of the peaks for IM bonded into the polymer chain (a), as end-group (b) and as free monomer (c). The * corresponds to remaining MeOH solvent.

With regard to the polycondensation reactions involving IIDMC monomer, the incorporation of the rigid sugar-based dimethyl ester was very successful in all cases with full incorporation of the IIDMC present in the comonomer mixture, as gathered in Table 1. A slightly higher mol% of IIDMC incorporated with respect to the mol% of IIDMC in the feed can be attributed to the volatilization of DMA comonomer during the reaction. The different reactivity and related feasibility of incorporating the two rigid bicyclic monomers, IM and IIDMC, into the polyesters with respect to the initial comonomer feed composition is most probably due to the selectivity on the active site of CALB. In fact, the active site of CALB is quite narrow for the diol unit and more accommodating for the acyl-donor side, in accordance with the observations made by Naik *et al.*[30] The ^{13}C NMR spectrum for entry **D** (Table 1) is depicted in Figure 2. For this series, ^{13}C NMR spectra showed complex signals for the 1,3-PD unit. The signal of the methylene group next to the oxygen of the propylene unit within the polyesters appears to be split into two peaks, corresponding to 1,3-PD units having an adipate unit as neighbor (61.4 ppm), or IIDMC as neighbor (62.3 ppm), with areas varying according to the polyester composition. It is also possible to observe the sensitiveness to the chemical environment at the quaternary carbon of the carbonyl group at 171-174 ppm, presenting two sets of signals, attributed either to the carbonyl of the adipate unit or to the carbonyl of the isoidide unit. Each set of peaks includes several signals related to the neighboring units, *i.e.* 1,3-PD and sorbitol (Figure S2).

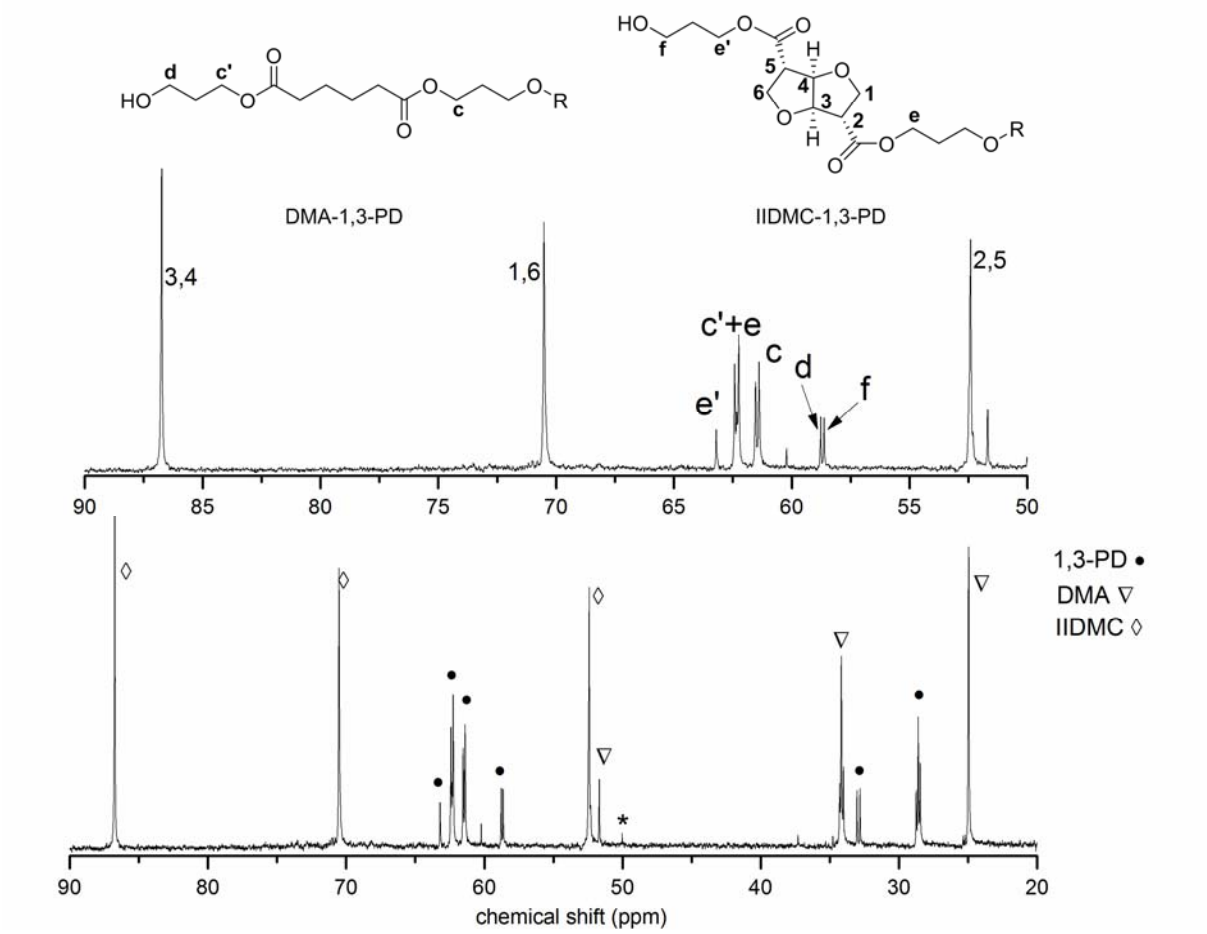


Figure 2. Section of inverse-gated decoupling ^{13}C NMR spectrum of entry **D** in Table 1 recorded in pyridine-d_5. Zoom of the region between 50 and 90 ppm and assignment of the peaks for 1,3-PD attached to adipate or to IIDMC units. The * corresponds to remaining MeOH solvent.

Through ^{13}C NMR analysis, the signals related to end-groups (OH, methyl ester and COOH) of the polymers were used to calculate the M_n of the obtained polyesters. Although dimethyl esters were used as acyl-donor moieties, the presence of a small peak related to carboxylic acid end-group is an indication that some hydrolysis during the polymerization reaction had occurred. From the end-group analysis it appears that, although there are signals attributed to methyl ester and carboxylic acid end-groups, the polyesters are mostly hydroxyl end-capped. The M_n calculated by NMR shows to be around 1.1 – 1.8 kg/mol, which is lower than the values determined by SEC. These discrepancies between the M_n determined *via* SEC and NMR are understood taking into account several factors. First of all, the calibration of SEC is based on poly(methyl methacrylate) standards, which have a significantly different hydrodynamic volume compared to the polyester samples. Besides, it has been observed in our previous study that the presence of sorbitol in the polymer chains can lead to hydrogen bonding between chains, thereby raising the apparent hydrodynamic volume of the chains in the SEC solvent, and also leading to a broadening of the molecular distribution.[5] Moreover, it is

known that, especially for aliphatic polyesters with M_n values lower than 10^4 g/mol, an overestimation of the M_n obtained *via* SEC measurements compared with the M_n obtained *via* ^{13}C NMR usually occurs.[32] Thus the main conclusion that can be drawn is that the molecular weights of the obtained sugar-based polyesters are appropriate for coating applications.

The evaluation in a quantitative manner of the total amount and different types of hydroxyl groups unreacted after polycondensation reactions is of great importance. The total amount of hydroxyl and carboxylic acid groups can be determined by potentiometric titration analysis.[33] However, this technique cannot distinguish between the different types of hydroxyl groups. Due to the unavailability of the high amounts of sample which are necessary to perform the potentiometric titration measurements in an accurate way, this determination has not been carried out in our present study. Notwithstanding, ^{31}P NMR spectroscopy is an effective method for evaluating not only the total amount of hydroxyl and carboxylic acid groups, but also at the same time can quantify the different types of hydroxyl (primary or secondary) and carboxylic acid groups present, whereas the amount of sample required for this technique is a couple of milligrams. As a spectroscopic technique, it is based on the different chemical environments of the observed nuclei after derivatization with a phospholane compound. A representative spectrum, including assignment of the most relevant peaks after derivatization of the polyester of entry **b** with the phospholane compound, is shown in Figure S3 for illustration. After derivatization, different hydroxyl and carboxylic acid groups appear with a deviated chemical shift, allowing assignment of the different primary hydroxyl end-groups coming from sorbitol and 1,3-PD, the secondary hydroxyl end-groups coming from IM, the secondary pendant hydroxyl groups from sorbitol, and carboxylic acid groups assigned to hydrolyzed IIDMC or adipate end-groups. In Table 2, the hydroxyl value (OHV) and acid value (AV) measured through ^{31}P NMR are expressed in mg KOH/g to facilitate later on the calculation for the curing reactions with polyisocyanates (*vide infra*).

Table 2. Acid (AV) and hydroxyl (OHV) values of the sugar-based polyesters.

Entry	Molar composition[a,b]		^{31}P NMR								
	Diester	Diol	AV (mg KOH/g)[c]		OH sorbitol (mg KOH/g)[c]		OH isomannide (mg KOH/g)[b]		OH 1,3-PD (mg KOH/g)[c]	OHV (mg KOH/g)[c]	Ratio Sec. *vs.* Prim. sorbitol
	Adipate	PD:Sorb	Adipate	IIDMC	Prim. OH	Sec. OH	End-group	Free			
a	49.0	47.6 : 3.4	1.5	0	10.0	57.4	0	0	17.0	85.9	5.7
	Adipate	PD:Sorb:**IM**									
b	58.0	34.8 : 3.5 : **3.7**	4.6	0	6.8	65.2	7.8	1.1	26.8	112.3	9.6
c	57.0	36.5 : 3.0 : **3.5**	4.1	0	8.1	64.2	4.6	0.7	33.0	114.7	7.9
d	57.8	20.1 : 4.3 : **17.8**	3.7	0	6.1	74.5	31.7	4.7	15.4	136.1	12.2
e	49.3	8.4 : 3.7 : **38.6**	5.8	0	5.1	62.0	22.1	5.6	5.2	105.8	12.2
f	52.8	0 : 5.0 : **42.2**	2.5	0	3.2	41.0	38.1	2.8	0	87.6	12.8
	IIDMC:Adipate	PD:Sorb									
B	**5.8** : 50.3	40.2 : 3.7	3.7	0.1	5.7	63.6	0	0	19.7	92.8	11.1
C	**13.0** : 45.4	38.9 : 2.7	2.1	0.2	4.0	57.5	0	0	17.4	81.2	14.4
D	**29.0** : 39.4	27.9 : 3.7	5.3	2.1	13.3	60.7	0	0	56.1	137.5	4.6
E	**45.1** : 11.5	39.8 : 3.6	1.0	1.3	5.1	59.9	0	0	16.1	83.4	11.7
F	**55.7** : 0	42.2 : 2.1	0	1.4	4.2	47.9	0	0	19.7	73.2	11.4
	IIDMC	**IM**									
g	**51**	**49**	0	2.6	0	0	31.9	0.7	0	35.2	-

[a]: PD = 1,3-propanediol; Sorb = sorbitol; IM = isomannide; IIDMC = isoidide ester. [b]: Molar composition in the copolyester as determined by ^{13}C NMR analysis performed after precipitation in MeOH. [c]: Data obtained by ^{31}P NMR after precipitation in MeOH.

As can be seen in Figure S3 for the series with IM as rigid unit, two peaks are observed at 145.5 and at 145.7 ppm corresponding to IM as free monomer and IM as end-group, respectively. ^{31}P NMR spectroscopy confirmed the presence of free IM, as detected *via* ^{13}C NMR analysis. An increased amount of IM end-group is detected when higher amounts of IM are incorporated into the polyester, with a small deviation for entry **e**, Table 2. It is worth to mention that, in the case of entry **d** in Table 2, with comparable molar ratio between IM and 1,3-PD residues in the polyester chains, the rigid unit appears to be present in higher an amount as end-group with respect to 1,3-PD. The presence of a double amount of hydroxyl end-groups from the IM unit with respect to 1,3-PD end groups is indicating that 1,3-PD is mostly incorporated within the polymer backbone, whereas IM is mostly present as end-group. These observed data are supporting the low reactivity of IM with respect to 1,3-PD in the lipase-catalyzed reactions. The presence of a peak related to carboxylic end groups is in accordance with the ^{13}C NMR spectroscopy data. In the case of reactions involving IIDMC dimethyl ester as the rigid monomer, in the region typical for carboxylic groups reacting with the phospholane

compound, two distinctive peaks can be observed at 134.8 and 135.2 ppm. These peaks are assigned to hydrolyzed adipate and IIDMC end-groups, respectively. Comparing the total OHV, it can be observed that for similar sorbitol contents the total OHV of the IM-containing series are slightly higher than for the IIDMC-containing series. The low reactivity of IM has been ascribed as the main reason for the dominant presence of this monomer as end-group, resulting in polyesters that are mostly hydroxyl end-capped. On the other hand, in the series involving the more reactive IIDMC as rigid unit, less hydroxyl groups are present as end-group.

Additionally, the ratio between the different unreacted hydroxyl groups of the sorbitol unit after polycondensation reactions can be evaluated. Although this analysis refers to the average of the observed phosphorylated hydroxyl groups, from our previous study we deducted that if the ratio between secondary and primary sorbitol hydroxyl groups is higher than 4, this will refer to sorbitol units incorporated on average mainly as a diol, leaving most of the secondary hydroxyl groups unreacted.[5] The same assessment has been applied for these newly synthesized polyesters, revealing a ratio of secondary to primary hydroxyl groups of the sorbitol unit higher than 4 in all cases (Table 2), confirming that sorbitol was reacting predominantly through its primary hydroxyl groups.

An extended reaction time for the IM-involving polycondensation reactions and a negative deviation of the incorporated amount of IM with respect to its initial molar feed have been ascribed to the different reactivity of CALB toward the different diols involved. In fact the low reactivity of CALB for bulky monomers bearing secondary hydroxyl groups, as IM, with respect to linear monomers, such as 1,3-PD and sorbitol, did not affect the high selectivity for primary toward secondary hydroxyl groups of the sorbitol unit. This was supported by the high ratio of secondary over primary hydroxyl groups of the sorbitol unit, being higher than 4 for all the reactions, and for many polycondensations the ratios were even higher than 10 (Table 2). The fact that in the enzyme-catalyzed polycondensation reactions IM is mostly incorporated as end-group into the polymer chains, implying that at least one of the secondary hydroxyls of IM has been esterified, while the secondary OH groups of sorbitol are remaining almost intact could be understood taking into account that the sorbitol unit has two primary OH groups which react much faster than any secondary OH. Once the IM monomer starts to react, which occurs after an extended time, the sorbitol units may have been mostly incorporated already into the polymer chains, not only as end-groups but even within the polyester chains with both reactive primary OH groups esterified. At that point, the steric hindrance associated with the secondary OH groups of IM present as free monomer may be lower than the steric hindrance associated with the secondary OH groups of the sorbitol units within an oligomeric chain already formed. This could explain that the secondary hydroxyls of incorporated sorbitol remain unreacted whereas at least one of the secondary

hydroxyls of IM is esterified. With this combination of monomers no other catalyst than a region-selective enzyme would be capable of providing such a fine distinction: esterifying in first instance the primary hydroxyls of sorbitol while leaving the secondary OH groups of the sorbitol unit unreacted but at the same time involving (at least one of) the secondary hydroxyl groups of the IM unit.

3.4. Thermal properties of sugar-based polyesters

The orientation of the hydroxyl groups in the isohexide monomers not only has a crucial influence on their reactivity but also on the physical properties of the related polymers, translated into distinct effects on the glass transition temperature and crystallinity.[18,19] In previous studies related to polymers derived from unmodified OH-functional isohexides, lower thermal stability has been observed for the *endo*-substituted isohexide-containing polymers. Isoidide showed to be the most stable isohexide, followed by isosorbide and IM.[31]

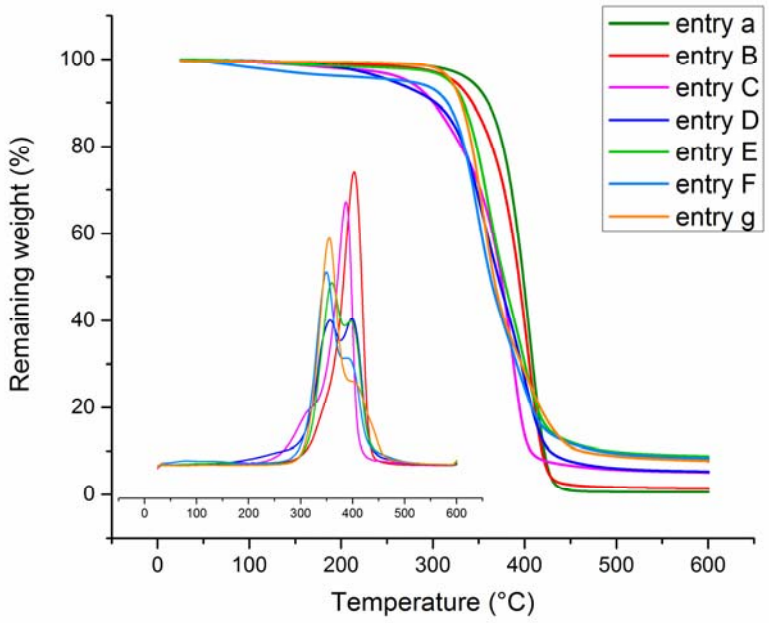


Figure 3. TGA traces of IIDMC-containing polyesters and compared derivative curves, recorded from 25 to 600 °C at a heating rate of 10°C/min under N_2 atmosphere.

The thermal behavior of the obtained enzymatically synthesized, sugar-based polyesters has been comparatively studied by Thermogravimetric Analysis (TGA) and Differential Scanning Calorimetry (DSC). TGA curves for the two series measured from 25 to 600 °C under nitrogen atmosphere are shown in Figure 3 and Figure S4, respectively. The thermal parameters resulting from these analyses are given in Table 3, where the corresponding data for the poly(propylene-*co*-sorbitol adipate) without rigid bicyclic units (entry **a**) are included for comparison. The IM-derived polyesters start to decompose at around 200-250 °C with an even lower stability for entry **f**, where 5% of its initial weight is already lost at 174 °C. However, the presence of free IM in these samples, detected *via* ^{13}C NMR,

may affect the thermal behavior and its sublimation is expected to be included in the 5% weight loss. Therefore, the comparison between the IM and IIDMC series will be made taking into account the temperature at which the degradation rate is maximum (Table 3). The IM-containing polyesters decomposed mainly in one step, with the temperature for maximum degradation rate (T_d) being between 400 and 425 °C (except for entry **e**, T_d = 352 °C), being also comparable to the polyester not containing any bicyclic units (entry **a**, T_d = 405 °C). For the IIDMC series two major decomposition steps occurred at approximately 350 and 400 °C, respectively. In fact, the remaining weight versus temperature plots are clearly showing the weight loss for each step based on the different acyl-moiety content, varying in accordance with the mol% of the two acyl units. It may be reasonably interpreted that the two decomposition steps observed for these copolyesters correspond to a first decomposition of bicyclic isoidide moieties followed by the adipate moieties. Also the fully isohexide-based polyester (entry **g**) decomposed in two steps, as previously reported by Wu *et al.* for the analogous polyester synthesized by metal-catalyzed polycondensation.[31] From these data it is shown that the adipate and 1,3-PD moieties decompose at a similar temperature as the IM moieties, *i.e.* with T_d around 400 °C, while IIDMC units decompose earlier, *i.e.* with T_d around 350 °C. For the differences in thermal stability of IM and IIDMC units, not only the different stereochemistry is playing a role, but also the different functionality, *i.e.* hydroxyl *vs.* acyl groups. Studies on hydroxyl and acyl-functional bicyclic moieties derived from acetalized sugars revealed the lower thermal stability of the corresponding polyesters when acyl-functional bicyclic acetalized units with respect to the hydroxyl-functional analogous were incorporated.[34] A residual weight up to 8% at 600 °C for the IM- and IIDMC-based polyesters is attributed to degradation products of the isohexide moieties, since it is known that linear poly(alkylene dicarboxylate)s decompose almost completely under the same TGA conditions.[35]

Table 3. Thermal properties of sugar-based polyesters.

Entry	Molar composition[a]		TGA			DSC
	Diester	Diol	$T_{5\%}$[b] (°C)	T_d[c] (°C)	W[d] (%)	T_g (°C)[e]
	Adipate	PD:Sorb				
a	49	47.6:3.4	342	405	1	-52
	Adipate	PD:Sorb:**IM**				
b	58.0	34.8 : 3.5 : **3.7**	226	402	1	-50
c	57.0	36.5 : 3.0 : **3.5**	217	401	1	-49
d	57.8	20.1 : 4.3 : **17.8**	243	410	2	-32
e	49.3	8.4 : 3.7 : **38.6**	250	352	4	-11
f	52.8	0 : 5.0 : **42.2**	174	425	2	4
	IIDMC:Adipate	PD:Sorb				
B	**5.8** : 50.3	40.2 : 3.7	323	345 / 403	1	-42
C	**13.0** : 45.4	38.9 : 2.7	264	316 / 387	5	-37
D	**29.0** : 39.4	27.9 : 3.7	278	357 / 399	5	-32
E	**45.1** : 11.5	39.8 : 3.6	318	360 / 398	8	2
F	**55.7** : 0	42.2 : 2.1	255	350 / 392	8	2
	IIDMC	**IM**				
g	**51**	**49**	320	355/403	8	28

[a]: PD = 1,3-propanediol; Sorb = sorbitol; IM = isomannide; IIDMC = isoidide dimethyl ester. [b]: Temperature at which 5% weight loss was observed; [c]: Temperature for maximum degradation rate; [d]: Residual weight at 600°; [e]: Glass transition temperature determined from the second heating curve of the DSC thermogram at a heating rate of 10 °C/min.

Thermal transitions were characterized by DSC and the obtained data are summarized in Table 3, while the second heating traces recorded from all sugar-based polyesters are depicted in Figure 4. All the precipitated polyesters were amorphous and showed a pronounced glass transition. To evaluate the effect of IIDMC incorporation on the glass-transition temperature with respect to IM, the two sets of polyesters have been compared allowing performing structure-thermal properties relations.

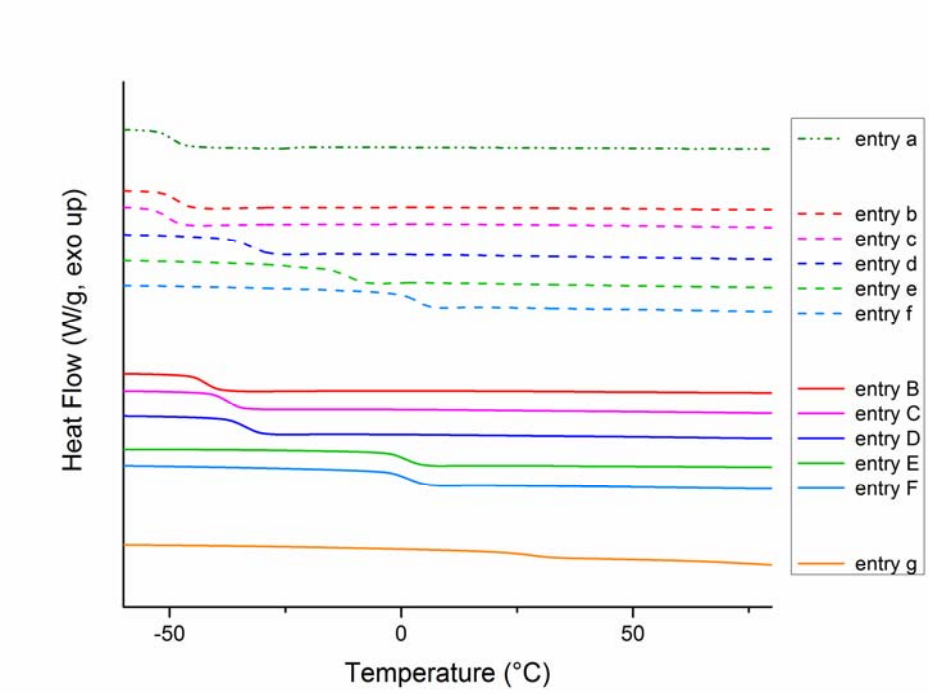
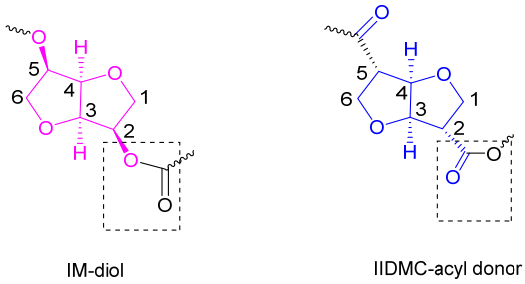


Figure 4. DSC traces from the second heating run of the sugar-based polyesters. The experiments were carried out from -80 °C to 100 °C at a heating rate of 10°C/min.

Two main structural differences can be observed between these isohexide monomers: the ester linkage at the bicyclic unit is reversed (Scheme 3), and the stereochemistry of the hydroxyl groups in the 2-5 positions is *endo-endo* for IM and *exo-exo* for IIDMC. Since the two series have comparable M_n, the effect on the T_g will be exclusively related to the amount of bicyclic units present in the polyesters without any effect due to different numbers of end-groups (resulting in different free volumes) or different degrees of entanglement formation.



Scheme 3. Structure of the compared isohexide moieties incorporated into the polyesters as diol (IM) or as acyl donor (IIDMC). The reversed ester linkage at the bicyclic unit is highlighted.

In both series, the presence of the isohexide unit induces rigidity into the polyester chains, resulting in an enhancement of the T_g with respect to the parent aliphatic sorbitol-containing polyester (entry **a**) of

about 50 °C. This increase of the T_g shows to be dependent on the content of the isohexide units, providing a well-controlled tuning of the thermal properties of the sorbitol-based polyesters synthetized by lipase-catalyzed polycondensation. A comparable increment has been observed by Wu *et al.* regarding polyesters synthesized *via* metal-based catalysis with respect to adipic-acid analogues.[35] Within this study, comparable results are presented by employing a more eco-friendly strategy such as metal-free, lipase-catalyzed polycondensation. Moreover, due to the high selectivity provided by CALB, pendant secondary hydroxyl groups coming from sorbitol units enhance the final hydroxyl functionality of the obtained isohexide-based polyesters, making them suitable for cross-linking and accordingly for coating applications.

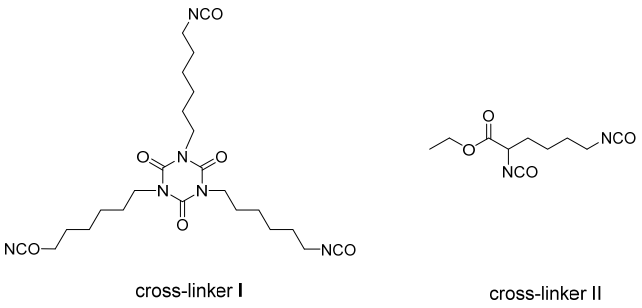
When comparing entries **d** and **D**, both having equal T_g, it appears that IM can introduce a slightly higher rigidity into the polyester main chain with respect to IIDMC, since the same T_g can be obtained with a slightly lower content of bicyclic sugar-based units. The observed behavior between the two different isohexides confirms the more flexible character of IIDMC with respect to IM. It has been previously argued by Wu *et al.* that ring puckering in the IIDMC conformation results in a kinked polymer chain that hinders close packing between polymer chains,[35] thereby raising the free volume and reducing the T_g, whereas packing is more tight for the IM conformation.

It can be concluded that both selected isohexide monomers, *i.e.* IM and IIDMC, are capable of increasing the T_g of the corresponding polyesters if compared with the parent polyester lacking isohexide units (entry **a**), the increase being slightly higher for IM than IIDMC. However, IIDMC showed to be more easily incorporated into the polyesters, providing a molar composition more in accordance with the feed ratio and resulting in shorter required reaction times with respect to IM.

3.5. Curing and coating evaluation of sugar-based polyesters

The sugar-based polyesters displayed M_n and hydroxyl functionalities adequate to be employed as polyester polyols for the synthesis of poly(ester-urethane)s. Their pendant hydroxyl groups along the backbone provided by the sorbitol units, as well as their terminal hydroxyl groups coming from 1,3-PD, sorbitol and IM units (if present), were made to react with polyisocyanates, resulting in cured poly(ester urethane) networks. For this preliminary evaluation, polyesters from entries **d**, **e**, **D** and **E**, having relatively high amounts of rigid monomer incorporated and high OHV, were selected, and compared to entry **a**. Due to thermal instability of polyester polyol **f** (*vide supra*), and the low OHV for entries **F** and **g**, those resins were not considered for this evaluation. The selected sugar-based polyester polyols were cured using both the petroleum-based isocyanurate trimer of hexamethylene diisocyanate, known as Desmodur N3600 (cross-linker I), as well as the bio-based ethyl ester L-lysine

diisocyanate (EELDI, cross-linker II), which is derived from L-lysine amino acid. The structures of the curing agents are depicted in Scheme 4. While the first curing agent is a cyclic trifunctional isocyanate, the latter is an aliphatic difunctional isocyanate. Although the synthetic route for the preparation of the isocyanate functionality still requires a petroleum-based compound, namely phosgene,[36] the carbon mass of the L-lysine amino acid-based EELDI is 75% renewable, which combined with fully bio-based polyesters provides cured coatings with a large renewable content. Moreover, previous studies have reported a variety of polyurethanes derived from bio-based L-lysine diisocyanate (LDI) to be biodegradable and non-toxic, and suitable to be used in biomedical applications.[37]



Scheme 4. Chemical structures of cross-linker I (Desmodur N3600) and cross-linker II (EELDI).

For the curing of all the polyester polyols, an NCO:OH ratio 1:1 was selected. Due to the bulkiness of the phospholane compound, a discrepancy between OHV derived from ^{31}P NMR measurements (OHV_{NMR}) and potentiometric titration has been observed earlier, with OHV being underestimated by the former technique with respect to the latter.[5,7] For the poly(propylene-*co*-sorbitol adipate) (entry **a**), the amount of sample available was enough for OHV determination by potentiometric titration (OHV_{PT}). The OHV_{PT} was found to be 123.8 mg KOH/g, which is 1.4 times higher than the OHV_{NMR} (Table 4). To take into account this effect, a 1.4 multiplication factor was applied to the OHV_{NMR}, and these estimated OHVs were used to calculate the amount of the curing agent required to have a ratio NCO:OH = 1:1 in all cases. To determine the appropriate curing conditions, the curing of a reaction mixture with NCO:OH ratio 1:1 of the potentially less reactive diisocyanate EELDI[38] with the polyester polyol **e** was monitored by FT-IR. By recording the decrease in intensity of the isocyanate absorption peak at 2271 cm^{-1} as a function of time, it was observed that after 10 min at 150 °C the isocyanate moiety of EELDI had fully reacted (Figure S5). Like the other polyester polyols synthesized in this study, even the most sensitive one, being polymer **e** in view of the presence of high amounts of unreacted monomer, showed to be stable (weight loss below 3% after one hour) at this temperature. Thus an extended time of 30 min was selected to ensure full curing of all hydroxyl groups. To prevent the final poly(ester urethane) coatings from containing any trace of metal contamination, the use of

catalysts to accelerate the reaction, e.g. dibutyltin dilaurate being one of the most common, has been avoided.

Since the sugar-based polyesters appeared to be highly hygroscopic, to preclude the isocyanates from reacting with moisture all the resins were kept in a vacuum oven before being employed in the preparation of solvent-cast coatings. Several polar solvents with boiling points below curing temperature have been tested (*viz.* acetone, THF, chloroform and cyclohexanone), among which chloroform produced the most satisfactory coatings in terms of appearance, except for polyester polyol **a**, where NMP was used as solvent. Upon curing of the polyester polyol/cross-linker mixtures onto the aluminum Q-panel substrates, the obtained poly(ester urethane) networks resulted in transparent colorless or slightly yellowish homogeneous films (Figure S6). These coatings were tested for solvent resistance, reverse impact resistance and pencil hardness. The coating formulations and their properties are listed in Table 4. Although a direct comparison between the poly(ester urethane) coatings from polyester polyol **a** and those containing rigid units (entries **d**, **e**, **D** and **E**) is not possible due to different curing conditions, *i.e.* different solvent and curing temperature (150 °C for entries **d**, **e**, **D** and **E**, and 180 °C for entry **a**), it is still relevant to correlate results obtained for different coatings. The T_g values of the poly(ester urethane) materials were determined *via* DSC measurements. In this case, the coatings were prepared from chloroform on a Teflon substrate and cured at 150 °C. Upon curing, an increased T_g with respect to the starting polyester is expected once the network is formed.

Polyester polyols **a** and **E** present comparable OHVs (thus also comparable number of urethane bonds in the poly(ester urethane) coatings) while containing either none or high mol% of rigid units (in this case IIDMC). As displayed in Table 4, curing of polyester polyols from entries **a** and **E** resulted in coatings with excellent solvent resistance. Through the reverse impact test, data concerning the ability of the material to cope with fast deformation are obtained. Some slight cracks were observed for formulation F1 (polyester polyol **a**, Desmodur N3600) and F2 (polyester polyol **a**, EELDI), mainly due to small defects of the coatings which affected the ability to resist rapid deformations. In spite of the higher thicknesses, which could lead to brittleness, the positive results of the impact resistance tests for F9 (polyester polyol **E**, Desmodur N3600) and F10 (polyester polyol **E**, EELDI) demonstrate that the obtained poly(ester urethane)s are sufficiently tough to withstand the rapid deformation. The hardness of the coatings was evaluated by the so-called pencil hardness test. Coatings F1 and F2 displayed hardness 2H and 2B, respectively, while a great improvement is observed for coatings F9 and F10, which showed much higher values (6H and 4H, respectively), reaching the characteristic range for a polyurethane-based coating.[39] This improvement can obviously be correlated to the

presence of bicyclic IIDMC units in the polymer chain for entry **E** with respect to entry **a**, demonstrating the effect of induced rigidity on the final material properties. In general an increased hardness is correlated with a higher T_g value, as can be observed in Table 4.

Table 4. Properties of poly(ester urethane) coatings obtained from the selected sugar-based polyesters.

Entry	IM/IIDMC (mol%)	OHV_{NMR} / OHV_{PT}[a] ($mg_{KOH}g^{-1}$)	T_g[b] (°C)	Film	Curing agent	Renewable (wt%)	Acetone resistance[c] (d.r. 75)	Impact test[d] (1 kg 80 cm)	Av. Film thickness (µm)	Pencil hardness[e]	T_g[f] (°C)
a	0 / 0	85.9 / 124	-52	F1	DES	71	+	+/-	30	2H	-32
				F2	EELDI	95	+	+/-	28	2B	-31
d	17.8 / 0	136.1 / 196	-32	F3	DES	61	+	+	41	5H	14
				F4	EELDI	93	+	+/-	93	5H	1
e	38.6 / 0	105.8 / 153	-11	F5	DES	67	+	+/-	62	6H	30
				F6	EELDI	94	+	+	54	5H	27
D	0 / 29.0	137.5 / 198	-32	F7	DES	61	+	+	54	3H	-10
				F8	EELDI	93	+/-	+	59	2H	-5
E	0 / 45.1	83.3 / 120	2	F9	DES	72	+	+	59	6H	11
				F10	EELDI	95	+	+	57	4H	5

DES = Desmodur N3600; EELDI = ethyl ester L-lysine diisocyanate. [a]: For entry **a**, OHV_{NMR} determined by ^{31}P NMR and OHV_{PT} obtained from potentiometric titration. For entries **d**, **e**, **D** and **E**, the OHV_{NMR} is measured and the OHV_{PT} is estimated based on the factor observed between OHV_{NMR} and OH_{PT} for entry **a**. [b]: Glass transition temperature before curing obtained *via* DSC. [c]:+ = good, +/- = moderate and - = poor. [d]: + = no damage, +/- =moderate damage, - = damaged. [e]: 6H to 2H= very hard to hard; H, F and B = moderately hard, 2B to 6B= soft to very soft. [f]: T_g obtained from DSC measurements after curing.

Whereas **a** and **E** had comparable and relatively low OHVs, on the other hand, polyester polyols **d** and **D** exhibited comparable but rather high OHVs and, thus, comparable cross-link density. A higher pencil hardness has been recorded for entry **d** (F3 and F4) than for entry **D** (F7 and F8), in accordance with higher rigidity given by the presence of IM or IIDMC unit in the polyester backbone, respectively, confirming a more rigid character of IM with respect to IIDMC (Table 4). In general a good behavior is recorded regarding the toughness of these coatings, since most of the poly(ester urethane)s obtained were able to withstand the reverse impact test. Only in the case of F4 (polyester polyol **d**, Desmodur N3600) and F5 (polyester polyol **d**, EELDI) the films presented small cracks after being tested, probably also due to the high thickness of the films. When comparing these polyester polyols cured with the same cross-linking agent, comparable cross-link densities could be expected, both being higher than for entry **a**, which exhibited a lower OHV.

When looking at similar mol% of rigid monomer incorporated, the most accurate comparison can be made by comparing polyester polyols **e** and **E**, with around 40 mol% of bicyclic units within the polyester polyols. Although a slightly lower mol% of bicyclic unit is present for entry **e** with respect to entry **E**, both cured networks reached a pencil hardness value between 4H and 6H, also depending

on the curing agent employed. However, a higher T_g was obtained for F5 (polyester polyol **e**, Desmodur N3600) and F6 (polyester **e**, EELDI) with respect to F9 (polyester polyol **E**, Desmodur N3600) and F10 (polyester polyol **E**, EELDI), which is most probably due to the higher OHV of entry **e** with respect to entry **E**, and therefore due to a higher amount of urethane bonds. Regarding the effect of the different cross-linkers on the final properties, the more rigid structure of Desmodur N3600 can contribute to a further increase of the hardness and the T_g of the cured material with respect to the bio-based cross-linker.

This study shows that successfully cured materials by using renewable polyester polyols containing bicyclic sugar-based units can be achieved. Moreover, the profound effect of the presence of the rigid bicyclic isohexide units on the final properties of the cured materials has been highlighted. Additionally, owing to the fully renewable character of the sugar-based polyester polyols used for the formulations, in the case EELDI is employed as curing agent the cured network is almost fully renewable. The obtained coatings, exhibiting a relatively hard character and good resistance against solvents and rapid deformations, can be suitable for an enlarged range of applications with respect to the reference coatings without isohexide units.

4. CONCLUSIONS

A novel series of polyesters based on renewable sorbitol and isohexide building blocks have been successfully synthesized for the first time *via* solvent-free lipase-catalyzed polycondensation. The selected isohexide-derived monomers, *viz.* isomannide (IM) and the recently developed isoidide dicarboxylic ester (IIDMC), have been incorporated as a diol or as acyl-donor, respectively, into the renewable polyesters. This approach yielded sugar-based polyesters with molecular weights and functionalities appropriate for coating applications. Despite the bulky character and the secondary OH functionality of the bicyclic IM structure, incorporation of this monomer was possible. However, the final mol% of IM incorporated was lower than the respective molar feed composition, the incorporation required very long reaction times, and IM was mostly incorporated as end-group in the polyester chain. Higher reactivity has been observed for IIDMC due to more adaptable acyl-pocket side of CALB, which allowed its incorporation in accordance with the initial feed and requiring shorter reaction times. As dimethyl ester moiety IIDMC shows to be a powerful platform for enzymatic polycondensation of isohexide-derived monomers. Furthermore, CALB showed its extraordinary versatile character, polymerizing in a highly selective way the multifunctional sorbitol mainly *via* its primary hydroxyl groups while leaving the secondary hydroxyl groups unreacted, but accepting a rigid monomer carrying only secondary hydroxyl groups such as IM. In both series, the presence of the isohexide units induced rigidity in the polyester chains, resulting in enhancement of the T_g with about

50 °C with respect to the parent sorbitol-based polyester lacking isohexide units, with slightly higher T_g values for the IM-derived polyesters. The isohexide and sorbitol-based polyesters were successfully utilized as polyester polyols in the preparation of poly(ester urethane)s coatings. When bio-based di-isocyanate EELDI is employed as curing agent, the obtained poly(ester urethane)s are a pragmatic example of close to fully renewable coatings. Since the curing process was carried out without the addition of any metal-based catalysts, the obtained coating materials are free from metal contamination and suitable to be used in biomedical applications. The increased rigidity of the obtained sugar-based polyesters was reflected in an increased hardness of the cured materials, thereby enlarging the possible application range of these fully bio-based aliphatic polyesters resins, which indeed exhibit some remarkable properties. This eco-friendly catalytic approach is a new contribution to make a further step in the development of tools, permitting the use of raw multi-functional carbohydrate-derived monomers for the manufacturing of sustainable materials.

ASSOCIATED CONTENT

Supporting information

^{13}C NMR spectra of IM- and IIDMC-containing polyesters, ^{31}P NMR spectrum of IM-containing polyester entry **b**, TGA curves of the IM-containing polyesters, FT-IR spectrum of the isocyanate kinetics and entry **e**, coating of sugar-based polyester on aluminum panel. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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REFERENCES

(1) Galbis, J. A.; Garcia-Martin, M. G.; Violante de Paz, M.; Galbis, E. *Chem. Rev.* **2016**, *116*, 1600-1636.
(2) Werpy, T. A.; Holladay, J. E.; White, J. F.; PNNL-14808, Pacific Northwest National Laboratory, Richland, WA. 2004, p 1-63.
(3) Fu, H.; Kulshrestha, A. S.; Gao, W.; Gross, R. A.; Baiardo, M.; Scandola, M. *Macromolecules* **2003**, *36*, 9804-9808.
(4) Kobayashi, S.; Uyama, H.; Tsujimoto, T.; Kuwabara, M. *Polymer preprints* **2007**, *48*, 830-831.
(5) Gustini, L.; Finzel, L.; Lavilla, C.; Noordover, B. A. J.; Hendrix, M. M. R. M.; Gehrels, C.; Koning, C. E. *ACS Sustainable Chem. Eng.* **2016**, *4*, 2259-2268.
(6) R. Sheldon, Green Chem. **2014**, *16*, 950-963.
(7) Gustini, L.; Lavilla, C.; Janssen, W. W. T. J.; Martínez de Ilarduya, A.; Muñoz-Guerra, S.; Koning, C. E. *Chem. Sus. Chem.* **2016**, *9*, 2250-2260.
(8) Lavilla, C.; Alla, A.; Martínez de Ilarduya, A.; Muñoz-Guerra, S. *Biomacromolecules* **2013**, *14*, 781-793.
(9) Japu, C.; Martínez de Ilarduya, A.; Alla, A.; Jiang, Y.; Loos, K., Muñoz-Guerra, S. *Biomacromolecules* **2015**, *16*, 868-879.
(10) Lavilla, C.; Gubbels, E.; Alla, A.; Martínez de Ilarduya, A.; Noordover, B. A. J.; Koning C. E.; Muñoz-Guerra, S. *Green Chem.* **2014**, *16*, 1789-1798.
(11) Kricheldorf, H. R. *Polym. Rev.* **1997**, *37*, 599-631.
(12) Noordover, B. A. J.; Van Staalduinen, V. G.; Duchateau, R.; Koning, C. E.; Van Benthem, R. A. T. M.; Mak, M.; Heise, A.; Frissen, A. E.; Van Haveren, J. *Biomacromolecules* **2006**, *7*, 3406-3416.
(13) Sablong, R.; Duchateau, R.; Koning, C. E.; de Wit, G.; van Es, D.; Koelewijn, R.; van Haveren, J. *Biomacromolecules* **2008**, *9*, 3090-3097.
(14) Kricheldorf, H. R.; Behnken, G.; Sell, M. *J. Macromol. Sci. Pure. Appl. Chem.* **2007**, *44*, 679, 684.
(15) Fenouillot, F.; Rousseau, A.; Colomines, G.; Saint-Loup, R.; Pascault, J. P. *Prog. Polym. Sci.* **2010**, *35*, 578- 622.
(16) Jasinska, L; Villani, M.; Wu, J.; van Es, D. S.; Klop, E.; Rastogi, S.; Koning, C. E. *Macromolecules* **2011**, *44*, 3458-3466.
(17) Bachmann, F.; Reimer, J.; Ruppenstein, M.; Thiem, J. *Macromol. Rapid Commun.* **1998**, *19*, 21-26.
(18) Pfeffer, J.; Ortel, M.; Spyrou, E.; Haas, T.; Korek, U.; Schmidt, H.; Dingerdissen, U. WO Patent 2011000585, **2011**.
(19) Wu, J.; Eduard, P.; Thiyagarajan, T.; van Haveren, J.; van Es, D.; Koning, C.E.; Lutz, M.; Foseca Guerra, C. *Chem. Sus. Chem.* **2011**, *4*, 599-603.
(20) Dais, P.; Spyros, A.; *Magn. Reson. Chem.* **2007**, *45*, 367-377.
(21) American Society for Testing and Materials (2010) Standard test method for resistance of organic coatings to the effects of rapid deformation (impact). D2794 − 93 (Reapproved 2010). ASTM, West Conshohocken.

(22) Anderson, E. M.; Larsson, K. M.; Kirk, O. *Biocatal. Biotransfor.* **1998**, *16*, 181-204.
(23) Linko, Y.-Y.; Wang, Z.-L.; Seppälä, J. *Enzyme Microb. Technol.* **1995**, *17*, 506-511.
(24) Mahapatro, A.; Kalra, B.; Kumar, A.; Gross, R. A. *Biomacromolecules* **2003**, *4*, 544-551.
(25) Léonard-Neversa, V.; Martona, Z.; Lamarea, S.; Hultb, K.; Grabera, M. *J. Mol. Catal. B: Enzymatic* **2009**, *59*, 90-95.
(26) Hæffner, F.; Norin, T.; Hult, K. *Biophys. J.* **1998**, *74*, 1251-1262.
(27) Anthonsen, T.; Hoff, B. H. *Chemistry and Physics of lipids* **1998**, *93*, 199-207.
(28) Hilker, I.; Rabani, G.; Verzijl, G. K. M.; Palmans, A. R. A.; Heise, A. *Angew. Chem. Int. Ed.* **2006**, *45*, 2130-2132.
(29) Habeych, D. I.; Juhl, P.B.; Pleiss, J.; Vanegas, D.; Eggink, G.; Boeriu, C. G. *J. Mol. Catal. B-Enzym.* **2011**, *71*, 1-9.
(30) Naik, S.; Basu, A.; Saikia, R.; Madan, B.; Paul, P.; Chaterjee, R.; Brask, J.; Svendsen, A. *J. Mol. Catal. B Enzym.* **2010**, *65*, 18-23.
(31) Wu, J.; Eduard, P.; Jasinska-Walc, L.; Rozanski, A.; Noordover, B. A. J.; van Es, D. S.; Koning, C. E. *Macromolecules* **2013**, *46*, 384-394.
(32) Garaleh, M.; Kricheldorf, H. R.; Weidner, S. M.; Yashiro, T. *J. Macromol Sci A: Pure Appl. Chem.* **2010**, *47*, 303-308.
(33) American Society for Testing and Materials (**2010**) Standard test methods for hydroxyl groups using acetic anhydride acetylation. ASTM E222-10. ASTM, West Conshohocken.
(34) Lavilla, C.; Alla, A.; Martínez de Ilarduya, A.; Benito, E.; García-Martín, M. G.; Galbis, J. A.; Muñoz-Guerra, S. *Polymer* **2012**, *53*, 3432-3445.
(35) Wu, J.; Eduard, P.; Thiyagarajan, S.; Jasinska-Walc, L.; Rozanski, A.; Fonseca Guerra, C.; Noordover, B. A. J.; van Haveren, J.; van Es, D. S.; Koning, C. E. *Macromolecules* **2012**, *45*, 5069-5080.
(36) Storey, R. F.; Wiggins, J. S.; Puckett, A. D. *J. Polym. Sci. A Polym. Chem.* **1994**, *32*, 2345-2363.
(37) Guelcher, S. A.; Gallagher, K. M.; Didier, J. E.; Klinedinst, D. B.; Doctor, J. S.; Goldstein, A. S.; Wilkes G. L.; Beckman, E. J.; Hollinger J. O. *Acta Biomater.* **2005**, *1*, 471-484.
(38) Li, Y.; Noordover, B. A. J.; van Benthem, R. A. T. M.; Koning, C. E. *ACS Sustainable Chem. Eng.* **2014**, *2*, 788-797.
(39) Gubbels, E.; Jasinska-Walc, L.; Noordover, B. A. J.; Koning, C. E. *Eur. Polym. J.* **2013**, *49*, 3188-3198.